

IN THE SPECIFICATION:

Please enter the changes in the specification indicated below:

At 1:2-5:

C1 This application claims the priority of U.S. Serial No. 09/303,375, filed April 30, 1999, U.S. Application No. 08/600,273, filed February 8, 1996, now US Pat. 5,958,406, is a continuation-in-part of U.S. Application No. 08/486,820 (continuation-in-part), filed June 7, 1995, now US Pat. 6,030,612, is a continuation-in-part of U.S. Application No. 08/385,540 (continuation-in-part), filed February 8, 1995, now US Pat. 5,945,102.

At 12:26 – 13:24:

Figs. 1A and 1B show the temperature stability of the poly-enzyme preparation of Example 1A when incubated at various temperatures over time scales of hours or days.

Fig. 2 shows the temperature optimum of the poly-enzyme preparation of Example 1A.

Fig. 3 shows the pH stability of the poly-enzyme preparation of Example 1A.

C2 **Fig. 4** shows the weight gain of mice having a soft ovarian-derived tumor that were either untreated or treated with the multifunctional enzyme purified as described in Example 1C.

~~**Fig. 5** shows the survival of the enzyme-treated and untreated mice containing the ovarian tumor.~~

Fig. 6 5 shows the increase in time between urinations for urinary bladder infection patients treated with a poly-enzyme preparation of Example 1A.

Fig. ~~7~~ 6 shows the reduction in erythema/swelling in patients with viral lung infections treated with the multifunctional enzyme purified as described in Example 1B.

Fig. ~~8~~ 7 shows the protective effect of the multifunctional enzyme, purified as described in Example 1C, against HIV.

Fig. ~~9~~ 8 shows the pH dependence of the multifunctional enzyme, purified as described in Example 1C, when tested against different substrates.

Fig. ~~10~~ 9 shows the titration of the activity of the multifunctional enzyme, purified as described in Example 1C, with 2 different protease inhibitors.

~~Fig. 11 shows the pain relief experienced by lame race horses treated with the poly enzyme preparation of Example 1A.~~

~~Fig. 12 shows certain indicators of healing following the treatment necrotic wounds with the multifunctional enzyme purified as described in Example 1B.~~

At 35:22 – 36:38 restore the following with the indicated changes:

The sequence of the first 25 amino acids of the Krill derived multifunctional enzyme is I-V-G-G-N/M-E-V-T-P-H-A-Y-P-(W)-Q-V-G-L-F-I-D-D-M-Y-F (SEQ ID NO. 4 20). The parentheses indicate a weak recovery of the 14th amino acid and "N/M" indicates heterogeneity at the 5th position. A comparison of the N-terminal 20 to 25 amino acid sequences of various serine hydrolases is presented in Table 2, below.

Table 2 - N-Terminal Sequences

<u>Species</u>	<u>SEQ ID NO</u>	<u>Sequence</u>
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<i>Penaeus vanameii</i> 1 (shrimp)	3	I V G G V E A T P H S W P H Q A A L F I D D M Y F
<i>Penaeus vanameii</i> 2	4	I V G G V E A T P H S X P H Q A A L F I
<i>P. monodon</i> , trypt. (shrimp)	5	I V G G T A V T P G E F P Y Q L S F Q D S I E G V
<i>P. monodon</i> , chym. 1	6	I V G G V E A V P G V W P Y Q A A L F I I D M Y F
<i>P. monodon</i> , chym. 2	7	I V G G V E A V P H S W P Y Q A A L F I I D M Y F
<i>Uca pugilator</i> I (crab)	8	I V G G V E A V P N S W P H Q A A L F I D D M Y F
<i>Uca pugilator</i> II	9	I V G G Q D A T P G Q F P Y Q L S F Q D
King crab	10	I V G G Q E A S P G S W P ? Q V G L F
Kamchatka crab	11	I V G G Q E A S P G S W P X Q V G L F F
	12	I V G G T E V T P G E I P Y Q L S L Q D
	13	I V G G T E V T P G E I P Y Q L S F Q D
	14	I V G G S E A T S G Q F P Y Q X S F Q D
Crayfish	15	I V G G T D A T L G E F P Y Q L S F Q N
krill Enzyme	1	I V G G N E V T P H A Y P W Q V G L F I D D M Y F
	2	I V G G M E V T P H A Y P W Q V G L F I D D M Y F
Bovine chymotrypsn	16	I V N G E D A V P G S W P W Q V S L Q D
Salmon	1917	I V G G Y E C K A Y S Q A Y Q V S L N S G Y H Y C
Atlant. Cod	1918	I V G G Y E C T K H S Q A H Q V S L N S G Y H Y C
Atlantic Cod	2019	I V G G Y E C T R H S Q A H Q V S L N S G Y H Y C

X = unknown or undefined.

At 40:10-30, restore the following that was inadvertently listed as deleted:

Example 1A - Poly-enzyme pr paration

03
Frozen krill were thawed and homogenized. An equal volume of distilled water containing 0.02% (w/v) sodium azide was added, and the admixture stirred for about 6 hours at about 4°C. Then, the supernate was collected by centrifugation. The supernate was defatted by adding ethyl acetate and stirring overnight at 4°C. The fat-containing ethyl acetate layer was then decanted and the aqueous extract evaporated sufficiently to remove the ethyl acetate. Ammonium sulfate was added to the extract to about 60% saturation at about 4°C and the mixture stirred overnight. The salted out precipitate was isolated by centrifugation. The precipitate was dissolved in phosphate buffered saline ("PBS", 0.05 M sodium phosphate, pH 7.4, 0.05 M sodium chloride) and dialyzed (using a 10 kd molecular weight cutoff) against PBS.

The redissolved precipitate was applied to a cross-linked agarose gel filtration column (Sephacryl 200, Pharmacia, Sweden) and the fractions displaying absorbance at about 280 nm were assayed for proteolytic activity. The combined proteolytically active fractions were pooled and lyophilized. A "poly-enzyme" preparation containing about six bands with apparent molecular weights (by SDS PAGE) ranging from 24 to 34 kd were isolated from antarctic krill in this way. For storage, a lyophilized powder of this preparation was aliquoted into ampules at 25 Casein Units per ampule.

At 42:27 – 43:11, restore the indicated sequence (previously deleted) and add the indicated sequence designation:

04
Samples of each preparation were analyzed by SDS-PAGE, and each preparation was found to contain a single protein that banded with apparent molecular weight of 29 kd. The SDS bands were electroblotted onto PVDF

C4
membranes and sequenced through 25 cycles of Edman degradation. See, Matsudaira, *J. Biol. Chem.*, 262: 10035-10038, 1987. Each preparation yielded the identical sequence: I V G G M / N E V T P H A Y P W Q V G L F I D D M Y F (SEQ ID No:20). Accordingly, it is clear that all three preparations are homogenous, although each is micro-heterogeneous at position 5. The proteolytic activity of each of the three preparations was tested against substrate benzoyl-val-gly-arg-p-nitroaniline. Hydrolysis of this substrate can be monitored at 210 nm, reflecting the release of p-nitroaniline. The pH-dependence of the three preparations at an ionic strength of 0.1 M is shown in Fig. 9 8. The profile for Prep-3 (shown with filled squares), Prep-8 (shown with open diamonds) and Prep-11 (shown with filled diamonds) are identical. All three had a pH optimum for this substrate of 9.5.

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SERIAL NO. 09/549,642

IN THE DRAWINGS:

Please cancel figures 5, 11 and 12, and revise prior figures 6-10 as attached to renumber them appropriately.

Ex. note ↗